

FIGURE 1: SEQ ID NO:1

Nucleotide Sequence Tankyrase homologue isotype1

CTTTGAAGACACTGGATTTTCATACTTTTGCCTGGGGTTATCTCTCTGTGTCTCACTACATAGACAAATA  
TTAGCTGTGAGCAGATCTTTTTTTTGTGCTTCTTGTAGTCCCCCAGTTTAGCAGAAACATTCTGTGAGA  
TAGATGTGGGAAAGGAATTCTAGCAAGAGTTTTGTCACTGTATCATAAGGTTGTGATTTACATATTTAA  
GTTTTATACTTTGAACATCTGAAAATGTATACATACTAAATATGCAGAACTCTATTGTAGAGTGAGAAA  
CATTTGAACCTTTGAGCTTTTCAGTCACTTATTTTGTATTCTTTCTTTGAGGTTAGCAGTAGTACCACCCA  
AGGCACTGCTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAGGTTTTGGGCG  
GAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAGTGTCCAAGCACGTGATGATGGGGGCCTTAT  
TCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCCTTTTGGCAGCATGGTGCAGA  
CCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAATTAAAGGAAAAGATTGATGT  
TTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAGATGGAAGGACAGCATTTGGA  
TTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAGATGAACCTTAGAAAGTGC  
CAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAATGTCAACTGCCACGCAAGTGA  
TGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAAAGATTGTACAGCTGTTACT  
GCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCATTACACAATGCCTGTTCTTA  
TGGTCATTATGAAGTAACTGAACCTTTTGGTCAAGCATGGTGCCTGTGTAAATGCAATGGACTTGTGGCA  
ATTCACCTCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTTCTCTCTTAAGTTATGG  
TGCAGACCCAACACTGCTCAATTGTGACAAATAAAGTGTCTATAGACTTGGCTCCACACCACAGTTAAA  
AGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCG  
AATCAAAAAACATCTCTCTCTGGAAATGGTGAATTTCAAGCATCCTCAAACACATGAAACAGCATTTGCA  
TTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAACCTGTGCTAAGAAAAGGAGCAAA  
CATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTGAGAAAGCTCATAATGATGT  
TGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACA  
CAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCCTACTCCTGAGCTATGGGTGTGATCCTAACAT  
TATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAATGTACAGCAACTCCTCCAAGAGGG  
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TCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGAATATCTGCTACAGCATGGAGCTGATGTGCA  
TGCTAAAGATAAAGGAGGCCTTGTACCTTTGCACAATGCATGTTCTTATGGACATTATGAAGTGCAGA  
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AGCAGCAAAAGGAAAATATGAAATTTGCAAACCTTCTGCTCCAGCATGGTGCAGACCTTACCAAAAAA  
CAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATATTCAAGATCTGCTTAGGGG  
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TTAGAAGTTGCAGATATTGTTTACAACACGGAGCTGATGTGAATGCCCAAGACAAAGGAGGACTTAT  
TCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTACTAATAAAGTATAATGCATG  
TGTCATATGCCACGGACAAATGGGCTTTACACCTTTGCACGAAGCAGCCCAAAGGGACGAACACAGCT  
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AACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTGATGATAAAGAGTTTCAGTC  
TGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCATGCAGGTGGAATCTTCAA  
CAGATACAATATTCTCAAGATTGAGAAGGTTTGTAAACAAGAACTATGGGAAAGATACACTCACCGGAG  
AAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTATTTTCATGGGTCTCCTTTTGT  
GAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCAT  
TTATTTTGTGTAACCTCTTCCAAAGCAATCAATATGTATATGGAATTGGAGGAGTACTGGGTGTCC  
AGTTCACAAAAGACAGATCTTGTACATTTGCCACAGGCAGCTGCTCTTTTGGCGGGTAACTTGGGAAA  
GTCTTTCTGTCAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTCATCACTCAGTCACTGGTAG  
GCCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAGAACAGGCTTATCCTGAGTA  
TTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAATAGTTATTTTAAGAACTA  
ATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTACTCCTTTGCTGAAAAAAA  
AA

FIGURE 2: SEQ ID NO:2

Nucleotide Sequence Tankyrase homologue isotype2

CGCGCTGCTCCGCCCGCCGCGGGGCGAGCCGGGGGGCAGGGAGCCCAGCGAGGGGCGCGCTGGGCGCGG  
 CCCATGGGACTGCGCCGGATCCGGTGACAGCAGGGAGCCAAGCGGCCCGGGCCCTGAGCGCGTCTTCTC  
 CGGGGGGCGCTCGCCCTCCTGCTCGCGGGGCGGGGCTCCTGCTCCGGTTGCTGGCGCTGTTGCTGGCTG  
 TGGCGGCGGCCAGGATCATGTGCGGTGCGCGCTGCGCCGGCGGGGGAGCGGCCTGCGCGAGCGCCGCGG  
 CCGAGGCCGTGGAGCCGGCGCCCGAGAGCTGTTGAGGCGTGCCGCAACGGGGACGTGGAACGAGTCA  
 AGAGGCTGGTGACGCCTGAGAAGGTGAACAGCCGCGACACGGCGGGCAGGAAATCCACCCCGCTGCACT  
 TCGCCCGAGGTTTTGGGCGGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCAC  
 GTGATGATGGGGGCTTATTCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCC  
 TTTTGGCAGATGGTGAGACCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAA  
 TTAAAGGAAAGATTGATGTTTTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAG  
 ATGGAAGGACAGCATTGGATTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAG  
 ATGAACTCTTAGAAAGTGCCAGGAGTGGAATGAAGAAAAAATGATGGCTCTACTCACACCATTAATG  
 TCAACTGCCACGCAAGTGATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAA  
 AGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCAT  
 TACACAATGCCTGTTCTTATGGTCATTATGAAGTAACCTGAACCTTTTGGTCAAGCATGGTGCCTGTGTAA  
 ATGCAATGGACTTGTGGCAATTCACCTCTCTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTT  
 CTCTTCTCTTAAGTTATGGTGAGACCCCAACTGCTCAATTGTGACAATAAAAGTGCTATAGACTTGG  
 CTCCACACCCACAGTTAAAAAGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCAC  
 GAGAAGCTGATGTTACTCGAATCAAAAAACATCTCTCTGGAATGGTGAATTTCAAGCATCCTCAAA  
 CACATGAAACAGCATTGCATTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAAGTGT  
 TGCTAAGAAAAGGAGCAACATCAATGAAAAGACTAAAGAATTTCTTGACTCCTCTGCACGTGGCATCTG  
 AGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAACATGAAGCAAAGGTTAATGCTCTGGATAATC  
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 ATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAATGTAC  
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 TTCAAGATCTGCTTAGGGGAGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGA  
 AGAAGTTGTCTTCTCCTGATAATGTAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATT  
 TAGCAGCTGGTTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCC  
 AAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTAC  
 TAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTACACCTTTGCACGAAGCAGCCC  
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 AAGGACAAACACCTTTAGATTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCC  
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 GGAGTTTTTTCAGAACTGTCTTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAA  
 AGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGG  
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 TTGGAATCAATGCTTATGGACATAGGCACAACTAATTAAAGGAGTCGAGAGACTTATCTCCGACAAC  
 AAGGTCTTAACCCATATTTAACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTG  
 ATGATAAAGAGTTTCAGTCTGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTC  
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 AAAGATACACTCACCGGAGAAAAGATTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTAT  
 TTCATGGGTCTCCTTTGTGAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTG  
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 GAGGAGTACTGGGTGTCCAGTTTCAAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTT  
 GCCGGGTAACTTTGGGAAAGTCTTTCTGTCAGTTTCAAGTGAATGAAATGGCACATTCTCCTCCAGGTC  
 ATCACTCAGTCACTGGTAGGCCCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAG  
 AACAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAA

TAGTTATTTTAAGAACTAATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTAC  
TCCTTTGCTGAAAAAAAAAAAA

FIGURE 3: SEQ ID NO:3

**Amino Acid Sequence Tankyrase homologue isotype1**

GFGRKDVVEYLLQNGASVQARDDGGLIPLHNACSFHAEVNNLLLRHGADPNARDNWNYPPLHEAAIKG  
KIDVCIVLLQHGAETIRNTDGR TALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNVNC  
HASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTPELLVKHGACVNAM  
DLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSALDLAPTQPKERLAYEFKGHSLQAAREA  
DVTRIKKHL SLEMVNFKHPQTHETALHCAAASYPYKPKQICELLRLKGANINEKTKEFLTPLHVASEKA  
HNDVVEVVVKHEAKVNALDNLGQTS LHRAAYCGHLQTCRLLLSYGCDPNIISLQGF TALQMGNE NVQQL  
LQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHG  
ADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAVNVADLWKFTPLHEAAAKGKYEICKLLLQHGADP  
TKKNRDGNTPLDLVKDGDTDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHLAA  
GYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQKG  
RTQLCALLLAHGADPTLKNQEGQTPDLVLSADDVSALLTAAMPSPALPSCYKPQVLNGVRSPGATADAL  
SSGPSSPSSL SAASSLDNLSGSFSELSSVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMDIF  
EREQITLDVLVEMGHKELKEIGINAYGHRHKLIGKVERLISGQQGLNPYLTLNTSGSGTILIDLSPDDK  
EFQSVVEEMQSTVREHRDGGHAGGIFNRYNLIKIQVCNKKLWERYTHRRKEVSEENHNHANERMLFHG  
SPFVNAI IHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFCRV  
TLGKSFLQFSAMKMAHSPPGHHSVTGRPSV

Bold = potential starting methionine

FIGURE 4: SEQ ID NO:4

**Amino Acid Sequence Tankyrase homologue isotype2**

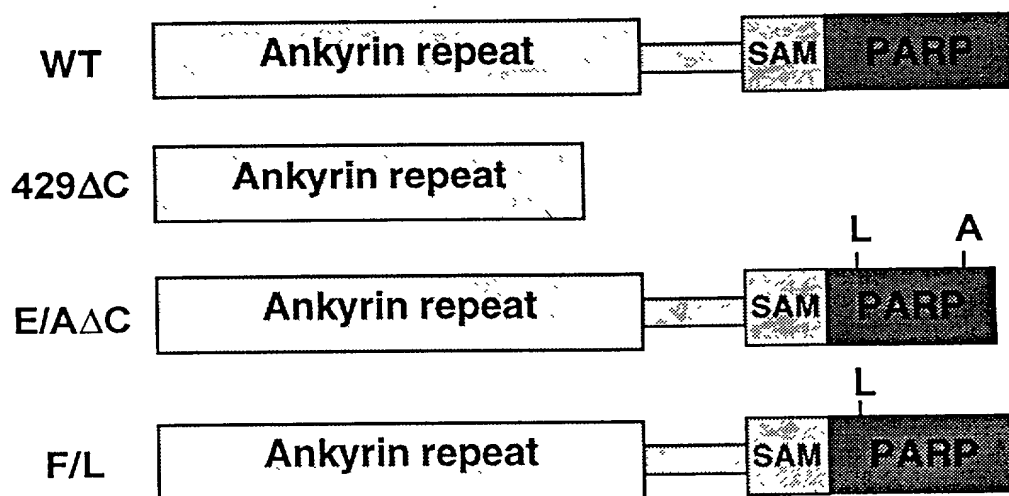
RCSARRGAAGGQGAQRGARVGA AHGTAPDPVTAGSQAARALSASSPGGLALLLAGPGLLLRLLALLLAV  
AAARIMSGRRRCAGGGAACASAAAEAVEPAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHF  
AAGFGRKDVVEYLLQNGANVQARDDGGLIPLHNACSFHAEVNNLLLRHGADPNARDNWNYPPLHEAAI  
KGKIDVCIVLLQHGAETIRNTDGR TALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNV  
NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTPELLVKHGACVN  
AMDWLQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSALDLAPTQPKERLAYEFKGHSLQAAR  
EADVTRIKKHL SLEMVNFKHPQTHETALHCAAASYPYKPKQICELLRLKGANINEKTKEFLTPLHVASE  
KAHNDVVEVVVKHEAKVNALDNLGQTS LHRAAYCGHLQTCRLLLSYGCDPNIISLQGF TALQMGNE NVQ  
QLLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQ  
HGADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAVNVADLWKFTPLHEAAAKGKYEICKLLLQHGA  
DPTTKKNRDGNTPLDLVKDGDTDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHL  
AAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQ  
KGRTQLCALLLAHGADPTLKNQEGQTPDLVLSADDVSALLTAAMPSPALPSCYKPQVLNGVRSPGATAD  
ALSSGPSSPSSL SAASSLDNLSGSFSELSSVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMD  
IFEREQITLDVLVEMGHKELKEIGINAYGHRHKLIGKVERLISGQQGLNPYLTLNTSGSGTILIDLSPD  
DKEFQSVVEEMQSTVREHRDGGHAGGIFNRYNLIKIQVCNKKLWERYTHRRKEVSEENHNHANERMLF  
HGSPFVNAI IHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFC  
RVTGKSFLQFSAMKMAHSPPGHHSVTGRPSV NGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDG

**FIGURE 5**

## Schematic Presentation of Dominant negative Mutants for Tankyrase Homologue

### Dominant Negative Mutants:

Truncation: 429 $\Delta$ C- of the C-terminal catalytic domain – truncation of the catalytic domain of PARP acts as a dominant negative when overexpressed *in vivo* (Oncogene 1999 Nov 25;18(50):7010-5)  
 Point mutant: E945A $\Delta$ C- conserved residue in PARP domain, thought to be important in NAD<sup>+</sup> binding



**FIGURE 6**

# **Cell Cycle Analysis of A549 Cells Infected With GFP-fused Wild Type and Mutant Tankyrase Homologue**

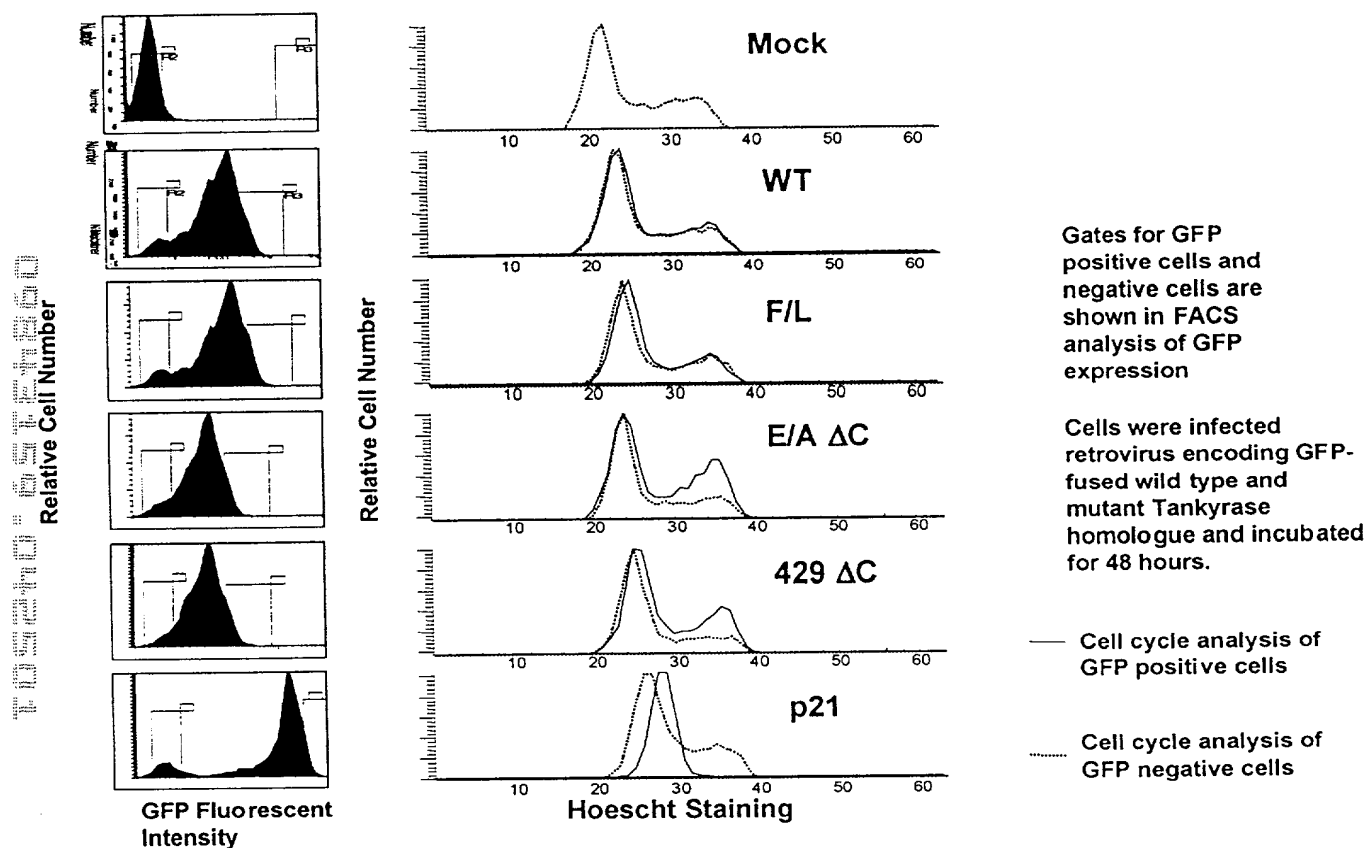
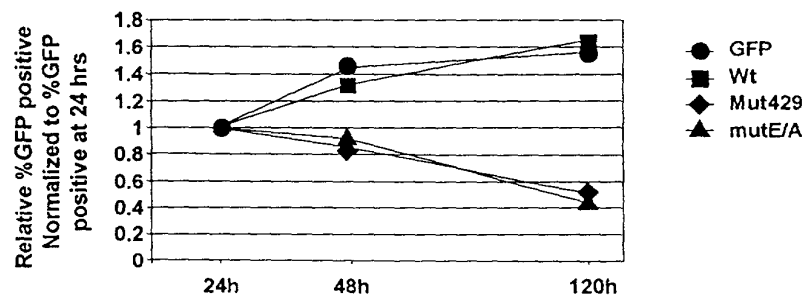


FIGURE 7

# Kinetics of GFP Positive cells in A549 Cells and Human Mammary Epithelial Cells(HMEC) After Retrovirus Infection Encoding GFP-fused Wild Type and Mutant Tankyrase Homologue

A549



HMEC

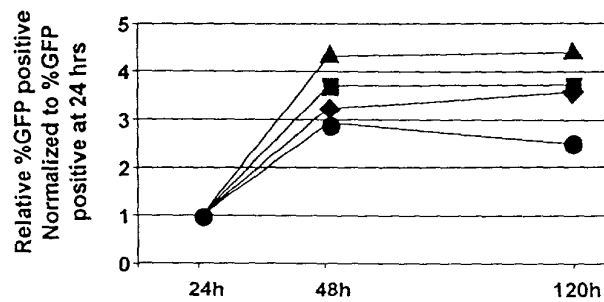
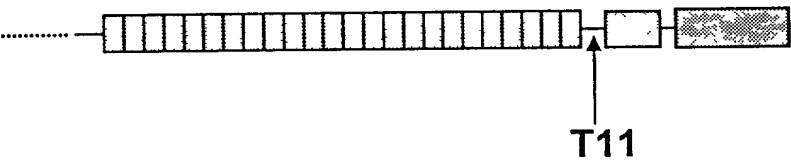


FIGURE 8

The Binding Site of Antisense Oligos Against Tankyrase Homologue

Tankyrase Homologue



□ Ankyrin repeat    ▨ SAM    ▩ PARP  
..... Unidentified sequence

T11

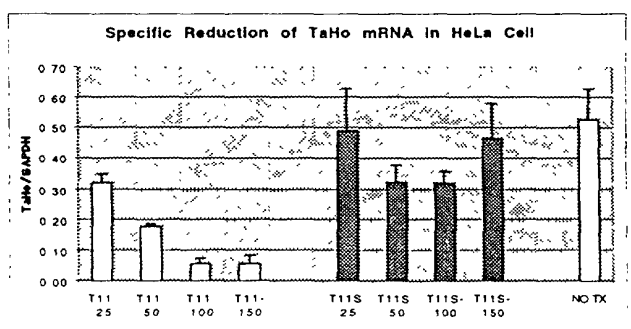
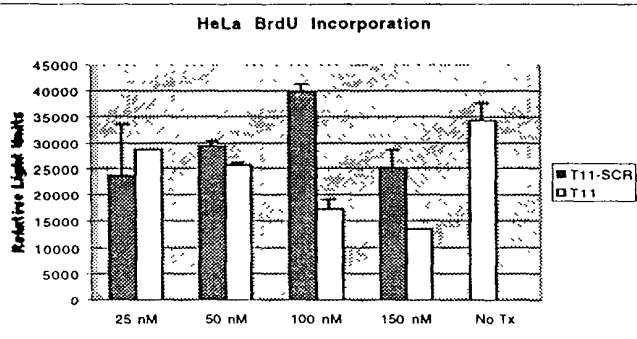
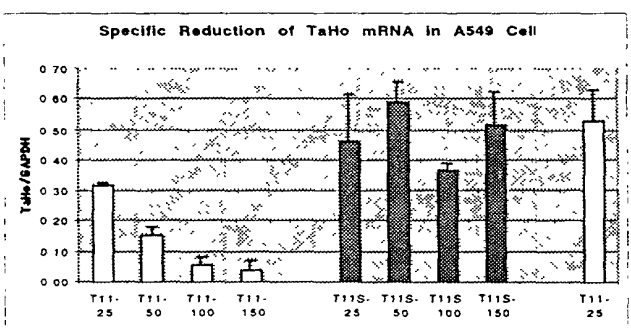
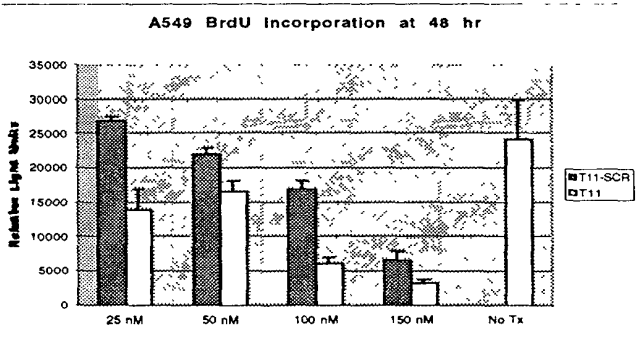
	GTGGAACAGAGGGTGCTTCC	
Tankyrase Homologue	GTGGAACAGAGGGTGCTTCCAGTTGGAGAAAAAGGAGGTTCCAGGAGTAGATTTTAGCAT	2838
Tankyrase	ATGCAGGGGATGGCGCCGCGGGAACAGAAAGGAAGGAGAAGTTGCTGGTCTTGACAT	3091
	***    *****    *	

FIGURE 9

# Anti-Proliferative Phenotype of Antisense Oligonucleotides Against Tankyrase Homologue in A549 and HeLa Cells

## Proliferation Analysis

## mRNA Analysis

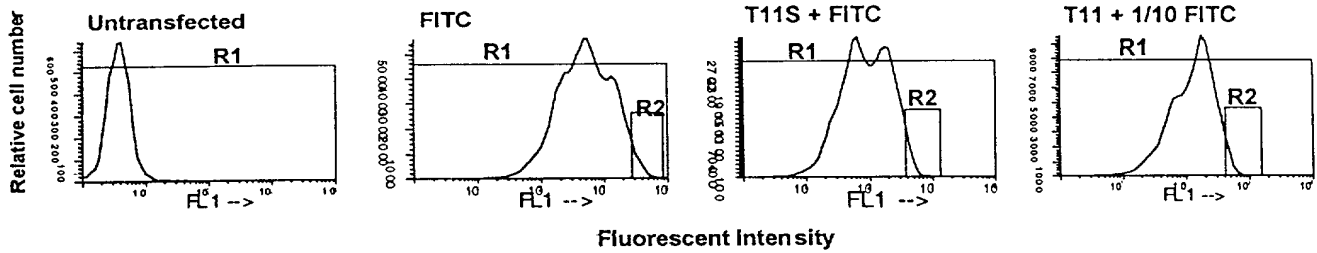




**FIGURE 10**

**Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and control oligonucleotides (T11S) were transfected with FITC-labeled random 20mer oligonucleotides(FITC), After 48 hours, entire population(R1) and top 5 % (R2)of FITC transfected cells were analyzed for cell cycle.**

**A) Gates for cell cycle analysis**



**B) Cell cycle analysis**

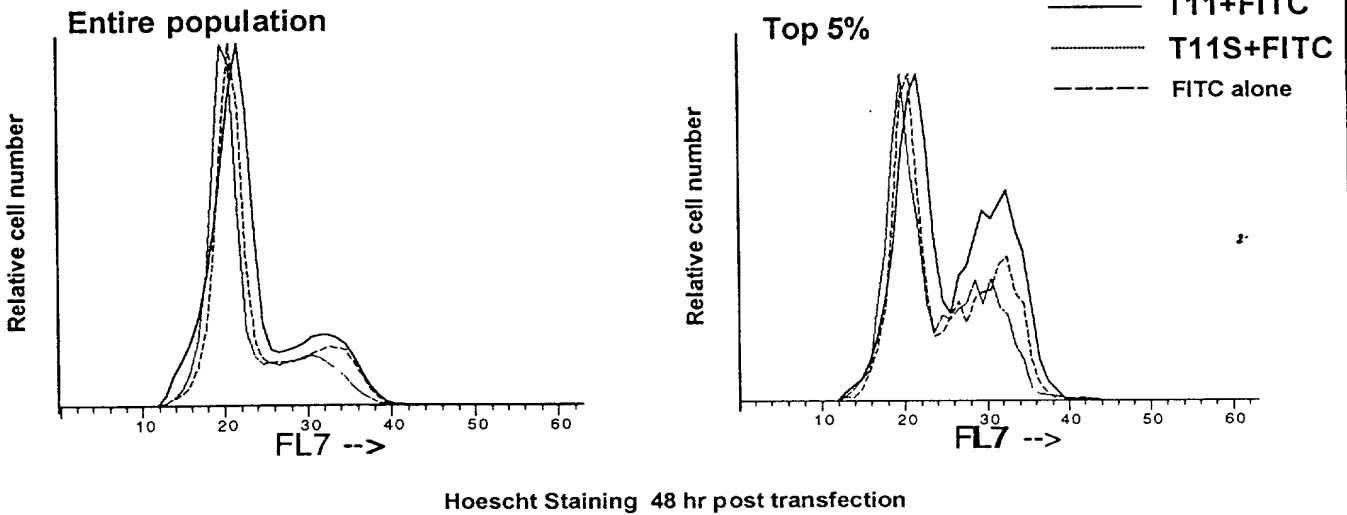
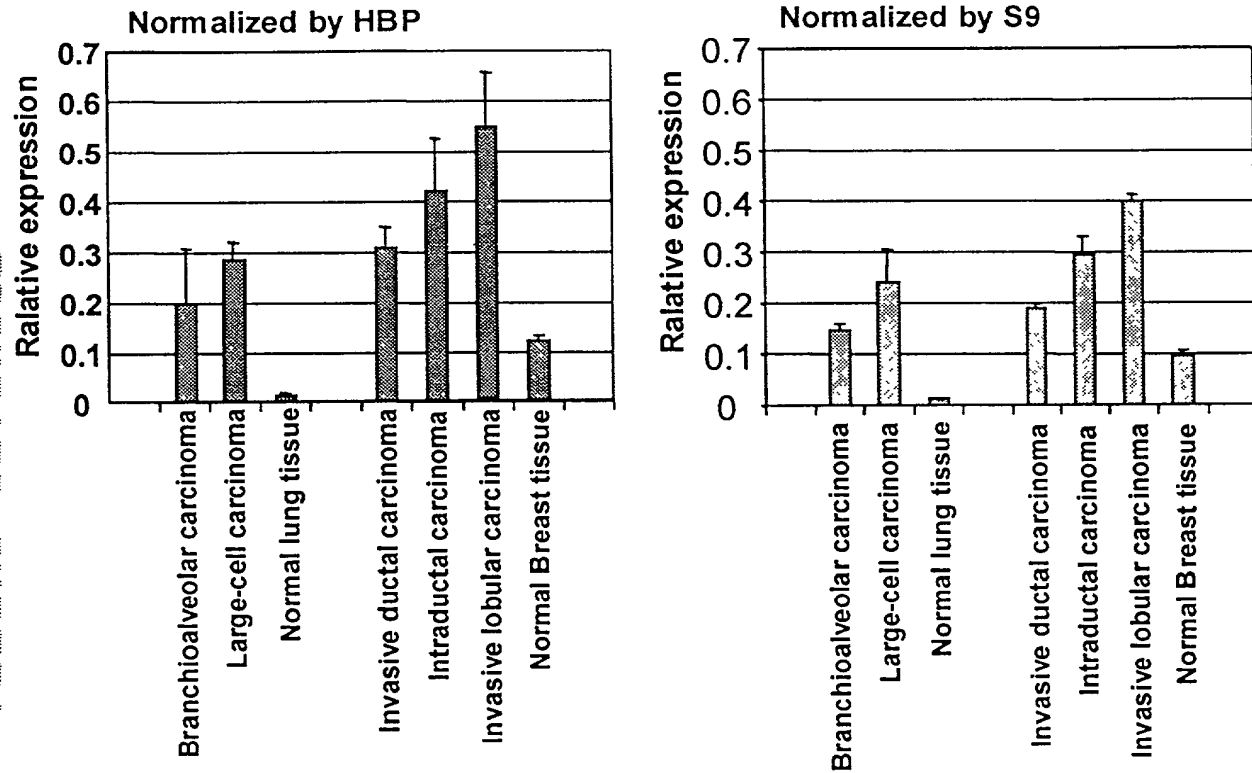


FIGURE 11

mRNA expression of Tankyrase Homologue in Several Tumors and Normal Tissues by a Taqman Analysis, mRNA expression was normalized by 90kDa Highly Basic Protein (HBP) and ribosomal protein S9 (S9).



**FIGURE 12**

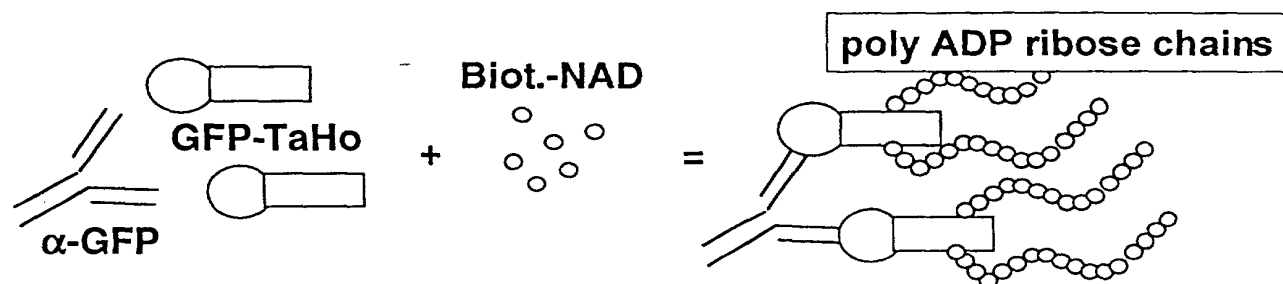
**Procedure for Nonisotopic Detection of Poly-ADP Ribosylation  
Using Anti-GFP mAb-Coated Plates**

Protein lysates from 293T cells normalized by GFP  
fluorescence and total protein

↓  
Immobilization of GFP-tankyrase homologue in anti-  
GFP Coated plates

↓  
Auto PARP reaction with Biotinylated-NAD in 96 wells

↓  
Detection of poly ADP ribose chains with Streptavidin-  
HRP and chemiluminescent substrate



**FIGURE 13**

**Non-Isotopic Plate-Based Detection of Taho PARP Activity in the Presence of Biotinylated NAD.**

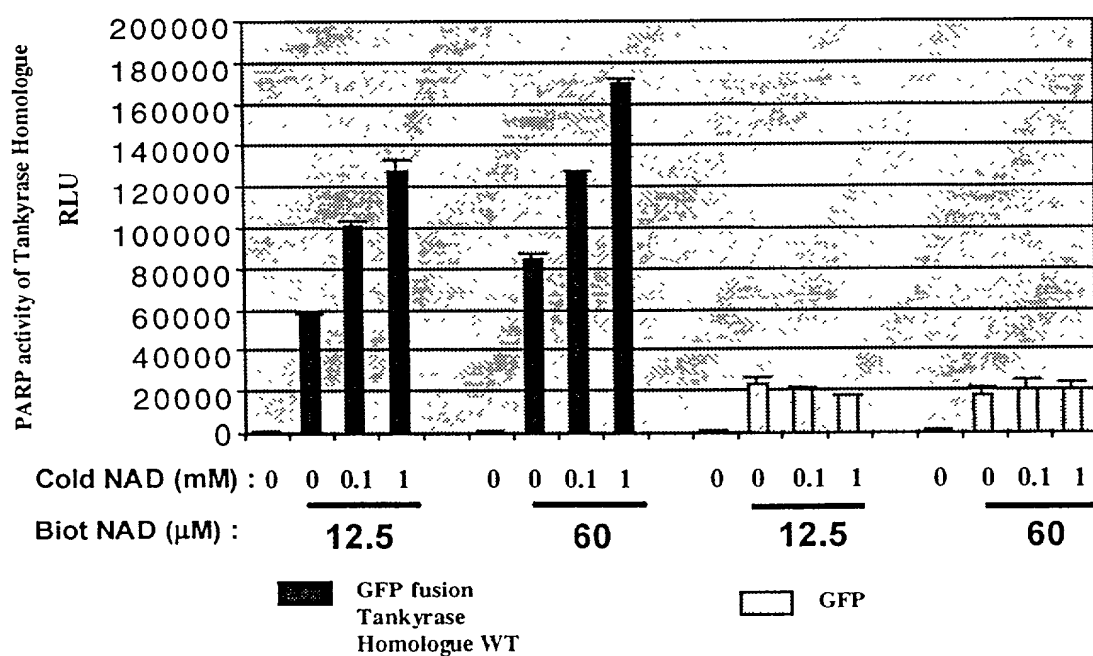


FIGURE 14

## Comparison of IC<sub>50</sub> Values of the PARP Inhibitors

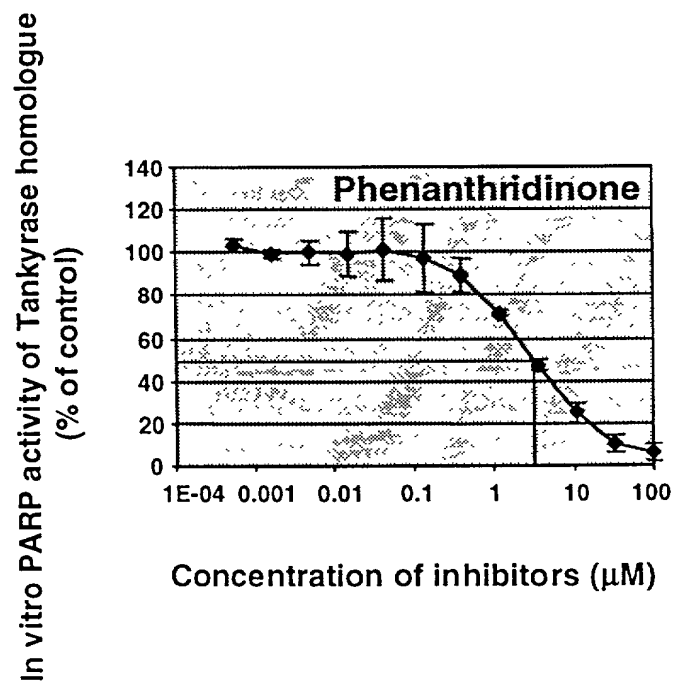
	Approximate IC <sub>50</sub> (nM)	hPARP assay IC <sub>50</sub> (nM)		
	<u>TaHo</u>	<u>Rigel</u>	<u>Decker</u> *	<u>Rankin</u> *
3AB	> 50 000	5 000	2 000	5 400
6(5H)Phenanthridinone	1 000-2 000	300		
Niacinamide	> 50 000	30 000	>>5 000	31 000

\* Decker P et al., *Clinical Cancer Research*. 1999 May; 5:1169-1172.

\* Rankin PW et al., *J Biol Chem*. 1989 Mar 15;264(8):4312-4317.

FIGURE 15

Inhibition of Tankyrase homologue PARP activity by hPARP inhibitors



TH-1: Tankyrase homologue isoform-1, TH-2: Tankyrase homologue isoform-2  
M (Red): the first methionine in the sequence, Z: stop codon  
In this figure, the first methionine in TH-1 sequence is position 1 (M1)

Taho C terminus deletion mutant ends at position 429 (K) and adds 28 amino acids because of frame shift.

Taho F/L mutant has the mutation at position 871

Taho E/A dC mutant has the mutation at position 948, ends at position 957 (A) and adds 2 amino acids.

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TH-1	-----	
TH-2	RCSARRGAAGGGAQARGAVGAAGTAPDPVTAGSQ	-231
TH-1	-----	
TH-2	AARALSASSPGLALLAGPGLLLRLALLLAVAAARIMSGRRRCAGGGAACASAAAEAVE	-171
TH-1	-----	
TH-2	PAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHFAAGFGRKDVVEYLLQNGA	-111
	Ankyrin repeat	Ankyrin repeat
TH-1	SVQARDGGLIPLHNACSFSGHAEVVNLLLRHGADPNARDNWNYPPLHEAAIKGKIDVCIV	-51
TH-2	NVQARDGGLIPLHNACSFSGHAEVVNLLLRHGADPNARDNWNYPPLHEAAIKGKIDVCIV	-51
	Ankyrin repeat	Ankyrin repeat
TH-1	LLQHGAETIRNTDGR TALDLADPSAKAVLTGEYKKDELLESARSNGEKKMMALLTPLNV	10
TH-2	LLQHGAETIRNTDGR TALDLADPSAKAVLTGEYKKDELLESARSNGEKKMMALLTPLNV	10

FIGURE 16  
(sheet 1 of 3)

	Ankyrin repeat	Ankyrin repeat
TH-1	NCHASDGRKSTPLHLAAGYNRVKIVQLLQLHGADVHAKDKGDLVPLHNACSYGHYEVT	70
TH-2	NCHASDGRKSTPLHLAAGYNRVKIVQLLQLHGADVHAKDKGDLVPLHNACSYGHYEVT	70
	Ankyrin repeat	Ankyrin repeat
TH-1	LVKHGACVNMADLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSAIDLAF	130
TH-2	LV	
	Ankyrin repeat	
TH-1	KERLAYEFKGHSLQLQAAREADVTRIKKHLSEMVFHKHPQTHETALHCAAASPYPKRKQI	190
	Ankyrin repeat	Ankyrin repeat
TH-1	CELLLRKGANINEKTKFETPLHVASEKAHNDVVEVVVKHEAKVNALDNLGQTS	250
	Ankyrin repeat	
TH-1	CGHLQTCRLLLSYGCDPNIISLQGFALQMGNEVQQLLEGISLGNSEADRLLEA	310
	Ankyrin repeat	Ankyrin repeat
TH-1	GDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHGADVHAKDKGGLVP	370
	Ankyrin repeat	Ankyrin repeat
TH-1	LHNACSYGHYEVAELLVKHGAVNVNADLWKFTPLHEAAAKGKYEICKLLQLHGADPTKKN	430
	Ankyrin repeat	Ankyrin repeat
TH-1	GMEILLWILLKMEIQIFKICLGEMQLCZ	
	RDGNTPLDLVKDGDFTDIQDLLRGDAALLDAKKGCLARVKKLSPPDNVNCRD	490
	Ankyrin repeat	

TH-1 LHNACSYGHYEVAELLVKHGAVNVNADLWKFTPLHEAAAKGKYEICKLLQLHGADPTKKN 430  
T  
Deletion--•



TH-1	LHLAAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATD 550 Ankyrin repeat Ankyrin repeat
TH-1	KWAF <sup>T</sup> PLHEAAQKGR <sup>T</sup> Q <sup>L</sup> CALLLAHGADPTLKNQEGQTPLDLVSADDDVSALLTAAMP <sup>S</sup> SA 610 Ankyrin repeat Ankyrin repeat
TH-1	LPSCYKPQVLNGVRSPGATADALSSGPPSSLSAASSLDNLSGSFSELSSVSSSGTEG 670 Ankyrin repeat
TH-1	ASSLEKKE--VPGVDFSITQFVRNLGLEHLMDFEREQITLDVLVEMGHKELKEIGINAY 730 SAM domain
TH-1	GHRHKLKIGVERLISGQQLNPYLTLNTSGSGTILIDLSPDDKEFQSV <sup>E</sup> EEEMQSTVREHR 790
TH-1	DGGHAGGIENRYN <sup>I</sup> LKIQVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFVN <sup>I</sup> AI 850
TH-1	HKG <sup>F</sup> DERHAYIGMFGAGIYFAENS <sup>S</sup> SKSNQYVYGIGGTGCPVHKDRSCYICHRQL <sup>L</sup> FCR 910 • F→L mutation PARP domain
TH-1	VTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNG <sup>L</sup> ALAEYVIYRGEQAYPEYLITYQIMRP 970 • E→A • Deletion. -----A-----LSZ
TH-1	EGMVDG 976